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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/979,518	04/10/2002	Judith E Meis	310307.90134	6310

7590 03/23/2007  
Jean C Baker  
Quarler & Brady  
411 East Wisconsin Avenue  
Milwaukee, WI 53202-4497

EXAMINER
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HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/23/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

# Office Action Summary

Application No.

09/979,518

Applicant(s)

MEIS, JUDITH E

Examiner

Richard G. Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 04 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 60,61,63,64,66 and 67 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 61,63 and 64 is/are rejected.
- 7) ☒ Claim(s) 60,66 and 67 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicant's amendment canceling claims 56-59, 62 and 65 and amending claims 60, 61, 63 and 64 and the addition of new claims 66 and 67, in the paper of 1/4/2007, is acknowledged. Claims 60, 61, 63, 64, 66 and 67 are present and at issue for examination.

Applicants' arguments filed on 1/4/2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Claim Objections***

Claims 60 and 61 (claims 63, 64, 66 and 67 dependent form) are objected to because of the following informalities:

Claims 60 and 61 (claims 63, 64, 66 and 67 dependent form) each recite "*Bacillus stearothermophilus* (Bst) type strain 5 in the presence of at least..." It is suggested that a comma or appropriate punctuation be placed after "strain 5" to improve the clarity of the claimed method.

Claims 60 and 61 (claims 63, 64, 66 and 67 dependent form) each recite "Bst DNA polymerase type strain 5". It is suggested that this should be "Bst type strain 5 DNA polymerase".

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61, 63 and 64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 59, and 61-65. In response to the rejection applicants have 59, 62 and 65, amended claims 61, 63 and 64 and added new claims 66 and 67 and traverse the rejection as it applies to the newly amended claims.

It is noted that applicants traverse this rejection under written description together with the rejection based on the scope of enablement.

Applicants traverse the rejection on the basis that applicants disagree with the previous statement by the examiner that the specification only provides the representative methods of use of that "DNA polymerase isolated from *B. stearothermophilus* strain ATCC 12980, encompassed by these claims". Applicants submit that the specification describes a specific and defined Bst DNA polymerase large fragment. Applicants further note that claim 61 defines the Bst DNA polymerase "large fragment" by both its size and its activity and applicants note that this purified large fragment is a result of a subtilisin digest also described in the specification.

Applicants submit that the limitation of claim 61 is based, in part on the following considerations: 1) subtilisin digests proteins at specific amino acid sequences; 2) the purified Bst DNA polymerase large fragment resulting from subtilisin digestion of the full-length Bst DNA polymerase encoded by *Bacillus stearothermophilus* (Bst) type strain 5 (ATCC strain number 12980) is a single band on a PAGE gel, consisting of a substantially homogeneous protein (sold by EPICENTRE Biotechnologies since 1994) and 3) the methods for making the protein by subtilisin digestion and further purification are described in the specification. Applicants further submit that the claimed methods for using both the full-length Bst DNA polymerase of claim 60 and the purified Bst DNA polymerase large fragment of claim 61 are also described in the "Examples" section of the specification.

Applicant's complete argument is acknowledged and has been carefully considered, however, continues to be found nonpersuasive for the reasons previously stated and for those repeated herein.

Applicants claimed methods continue to lack adequate written description for those DNA polymerases derived from *Bacillus stearothermophilus* (Bst) type strain 5, wherein the purified DNA polymerase is the product of any subtilisin digestion and is any truncated large fragment of any full-length Bst DNA polymerase type strain 5, wherein said fragment has a mass of about 55 to about 65 kDa, lacks 5' to 3' exonuclease activity and has reverse transcriptase activity in the presence of magnesium ions and in the substantial absence of manganese ions. As the only structural limitations of the recited DNA polymerase are that it has a mass of about 55 to

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about 65 kDa and is any truncated large fragment of any full-length Bst DNA polymerase type strain 5, the polymerases of the claimed method remain inadequately described. Especially in light of applicants recitation that the claimed DNA polymerase is derived from a *Bacillus stearothermophilus* strain and most organisms have multiple different DNA polymerases.

The specification continues to only provide the representative methods of use of that DNA polymerase isolated from *B. stearothermophilus* strain ATCC number 12980, encompassed by these claims. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

Claims 61, 63 and 64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed amplification /synthesis methods using the DNA polymerase from strain ATCC No. 12980, does not reasonably provide enablement for the claimed methods of amplification/synthesis using any DNA polymerase derived from *B. stearothermophilus* type strain 5, wherein the DNA polymerase is the product of any subtilisin digestion and is any truncated large fragment of any full-length Bst DNA polymerase type strain 5, wherein said fragment has a mass

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of about 55 to about 65 kDa, lacks 5' to 3' exonuclease activity and has reverse transcriptase activity in the presence of magnesium ions and in the substantial absence of manganese ions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 59, and 61-65. In response to the rejection applicants have 59, 62 and 65, amended claims 61, 63 and 64 and added new claims 66 and 67 and traverse the rejection as it applies to the newly amended claims.

It is noted that applicants traverse this rejection based on a lack of scope of enablement together with the above rejection based on inadequate written description.

Applicants traverse the rejection as discussed above, on the basis that applicants disagree with the previous statement by the examiner that the specification only provides the representative methods of use of that "DNA polymerase isolated from *B. stearothermophilus* strain ATCC 12980, encompassed by these claims". Applicants submit that the specification describes a specific and defined Bst DNA polymerase large fragment. Applicants further note that claim 61 defines the Bst DNA polymerase "large fragment" by both its size and its activity and applicants note that this purified large fragment is a result of a subtilisin digest also described in the specification.

Applicants submit that the limitation of claim 61 is based, in part on the following considerations: 1) subtilisin digests proteins at specific amino acid sequences; 2) the purified Bst DNA polymerase large fragment resulting from subtilisin digestion of the full-

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length Bst DNA polymerase encoded by *Bacillus stearothermophilus* (Bst) type strain 5 (ATCC strain number 12980) is a single band on a PAGE gel, consisting of a substantially homogeneous protein (sold by EPICENTRE Biotechnologies since 1994) and 3) the methods for making the protein by subtilisin digestion and further purification are described in the specification. Applicants further submit that the claimed methods for using both the full-length Bst DNA polymerase of claim 60 and the purified Bst DNA polymerase large fragment of claim 61 are also described in the "Examples" section of the specification.

As above, applicant's complete argument is acknowledged and has been carefully considered, however, continues to be found nonpersuasive for the reasons previously stated and for those repeated herein.

Applicants claimed methods continue to be so broad as to encompass any DNA polymerase derived from *Bacillus stearothermophilus* (Bst) type strain 5, wherein the purified DNA polymerase is the product of any subtilisin digestion and is any truncated large fragment of any full-length Bst DNA polymerase type strain 5, wherein said fragment has a mass of about 55 to about 65 kDa, lacks 5' to 3' exonuclease activity and has reverse transcriptase activity in the presence of magnesium ions and in the substantial absence of manganese ions. As the only structural limitations of the recited DNA polymerase are that it has a mass of about 55 to about 65 kDa and is any truncated large fragment of any full-length Bst DNA polymerase type strain 5, the polymerases of the claimed method remain sufficiently broad that the full scope of the genus lacks enablement. Especially in light of applicants recitation that the claimed



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DNA polymerase is derived from a *Bacillus stearothermophilus* strain and most organisms have multiple different DNA polymerases, which could potentially be used to derive the DNA polymerases encompassed by the claimed methods.

The specification does not support the broad scope of the claims which encompass all methods of use of any modifications and fragment of any *B. stearothermophilus* DNA polymerase encompassed by the claims, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting polymerase activity; (B) the general tolerance of *B. stearothermophilus* DNA polymerases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a *B. stearothermophilus* DNA polymerase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the *B. stearothermophilus* DNA polymerase, 5'-3' exonuclease and reverse transcriptase activities necessary to practice the claimed methods and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those methods of use of any DNA polymerase derived from *B. stearothermophilus* type strain 5.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including method of use of any number of amino acid modifications of any *B. stearothermophilus* derived DNA polymerase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those DNA polymerases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

### **Conclusion**

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'R. G. Hutson', with a long horizontal line extending to the right.

Richard G Hutson, Ph.D.  
Primary Examiner  
Art Unit 1652

rg  
3/15/2007